Why Beagles Are a Poor Model for Drug Development

Beagles are commonly used in preclinical drug testing, particularly for toxicology studies, due to their docile nature, manageable size, and historical regulatory requirements. However, they are increasingly recognized as inadequate models for predicting human responses to drugs. Here are the key reasons, based on scientific evaluations:

Significant Species Differences in Physiology and Metabolism:

1. Beagles (and dogs in general) exhibit notable biological variances from humans, such as differences in drug metabolism, absorption, and organ function. For instance, dogs have poorer acid secretion in the stomach compared to humans, which can lead to inaccurate assessments of pH-dependent drug formulations.
2. This results in poor predictions of oral bioavailability and absorption rates; one study of 43 drugs found only a weak correlation
3. Broader research highlights that animal models, including dogs, fail to reliably predict human toxicities due to these interspecies gaps.

Low Predictive Value for Human Outcomes:

1. Preclinical animal studies, including those using beagles, have a poor track record in forecasting human efficacy and safety.
2. Studies show that animal experiments predict human reactions only about 70% of the time or less, leading to high failure rates in clinical trials—over 90% of drugs that pass animal tests fail in humans.
3. Specifically for beagles, their genetic homozygosity (inbred strains) makes them a poor proxy not just for humans but even for other dog breeds, limiting their utility in toxicity predictions.

Regulatory and Practical Limitations:

1. While beagles are favored for non-rodent studies under outdated FDA guidelines, emerging evidence and policy shifts (like the FDA's 2025 plan to phase out animal testing) underscore their obsolescence.
2. Animal models often overestimate or underestimate risks, contributing to inefficient drug development pipelines.
3. These issues aren't unique to beagles but are amplified in their use for drug development, where precise human relevance is critical.

References for "Why Beagles Are a Poor Model for Drug Development"

Below is a compiled reference list of sources that support the key elements of the document, including species differences in physiology and metabolism, low predictive value of animal models, genetic factors in beagles, and regulatory shifts toward reducing animal testing. These are drawn from scientific publications and reports as of early 2026.

Significant Species Differences in Physiology and Metabolism

Dogs exhibit differences in drug metabolism, absorption, and organ function compared to humans, such as variations in cytochrome P450 enzymes and gastrointestinal physiology.

Bogaards, J. J., et al. (2006). Species differences between mouse, rat, dog, monkey and human CYP-mediated drug metabolism, inhibition and induction. Expert Opinion on Drug Metabolism & Toxicology.
https://pubmed.ncbi.nlm.nih.gov/17125407/

Canine physiological factors, including drug transporter activity and specificity, differ from humans, impacting pharmacokinetic predictions.

Martinez, M. N., et al. (2021). Comparison of Canine and Human Physiological Factors: Understanding Interspecies Differences that Impact Drug Pharmacokinetics. Toxicological Sciences.
https://pubmed.ncbi.nlm.nih.gov/33907906/

A study of 43 drugs showed only a weak correlation in oral absorption between dogs and humans, with 22 drugs fully absorbed in both but overall poor predictability.

Chiou, W. L., et al. (2000). Evaluation of using dog as an animal model to study the fraction of oral dose absorbed of 43 drugs in humans. Pharmaceutical Research. https://pubmed.ncbi.nlm.nih.gov/10751026/

Differences in benzodiazepine metabolism and tissue distribution are more rapid in dogs than in humans.

Klotz, U. (1983). Comparative pharmacokinetics of benzodiazepines in dog and man. Journal of Pharmacokinetics and Biopharmaceutics.
https://pubmed.ncbi.nlm.nih.gov/6130139/

Breed-specific variations in drug pharmacokinetics and metabolism in dogs highlight limitations in using them as models for human responses.

Fleischer, S., et al. (2008). Pharmacogenetic and Metabolic Differences Between Dog Breeds: Their Impact on Canine Medicine and the Use of the Dog as a Preclinical Animal Model. The AAPS Journal.
https://pmc.ncbi.nlm.nih.gov/articles/PMC2747081/

Low Predictive Value for Human Outcomes

Animal models, including dogs, have poor predictive value for human toxicities, with failure rates exceeding 90% for drugs passing preclinical tests.

Van Norman, G. A. (2019). Limitations of Animal Studies for Predicting Toxicity in Clinical Trials: Is it Time to Rethink Our Current Approach? JACC: Basic to Translational Science.
https://pmc.ncbi.nlm.nih.gov/articles/PMC6978558/

Preclinical animal studies predict human reactions only about 50-70% of the time, contributing to high clinical trial failure rates.

Monticello, T. M., et al. (2020). Pre-clinical animal models are poor predictors of human toxicities in phase 1 oncology clinical trials. British Journal of Cancer.
https://www.nature.com/articles/s41416-020-01033-x

Approximately 90% of drug candidates that pass animal studies fail in human trials due to species differences and poor translatability.

Arrowsmith, J., et al. (2015). New Approach Methodologies in Drug Development. Drug Discovery Today.
https://www.sciencedirect.com/science/article/abs/pii/S1359644625001886

Animal models often fail to predict human efficacy and safety, with examples like gene therapies causing issues in humans despite animal success.

Van Norman, G. A. (2024). The (misleading) role of animal models in drug development. Frontiers in Drug Discovery.
https://www.frontiersin.org/journals/drug-discovery/articles/10.3389/fddsv.2024.1355044/full

In oncology, phase II success rates are around 25%, often due to efficacy failures not detected in animal models.
nc3rs.org.uk
NC3Rs. (2023). Improving the predictive power of models for cancer research.
https://nc3rs.org.uk/our-portfolio/improving-predictive-power-models-cancer-research

Genetic Factors in Laboratory Beagles

Laboratory beagles show restricted DLA class II haplotypes and higher homozygosity (up to 28.4% across breeds), limiting their representativeness for diverse human populations.sciencedirect.com
Kennedy, L. J., et al. (2015). Restricted dog leucocyte antigen (DLA) class II haplotypes and genotypes in Beagles. The Veterinary Journal.
https://www.sciencedirect.com/science/article/pii/S1090023314005309

Genetic diversity analysis in beagle populations reveals low inbreeding but highlights the impact of homozygosity on their use as models.pmc.ncbi.nlm.nih.gov
Kim, J. H., et al. (2025). An Analysis of the Genetic Diversity, Genetic Structure, and Selection Signal of Beagle Dogs Using SNP Chips. Animals.
https://pmc.ncbi.nlm.nih.gov/articles/PMC12026597

Regions of homozygosity in beagles, the preferred breed for drug development, reduce their utility in predicting human toxicities due to genetic uniformity.biorxiv.org
Dreger, D. L., et al. (2020). Using regions of homozygosity to evaluate the use of dogs as preclinical models in human drug development. bioRxiv.
https://www.biorxiv.org/content/10.1101/2020.01.08.898916v1

Regulatory and Practical Limitations

The FDA's 2025 plan outlines phasing out animal testing requirements over 3-5 years, making it the exception for preclinical safety studies.fda.gov
FDA. (2025). FDA Announces Plan to Phase Out Animal Testing Requirement for Monoclonal Antibodies and Other Drugs.
https://www.fda.gov/news-events/press-announcements/fda-announces-plan-phase-out-animal-testing-requirement-monoclonal-antibodies-and-other-drugs

FDA roadmap aims to reduce animal use in toxicity testing through alternatives, addressing the obsolescence of models like beagles.fda.gov
FDA. (2025). Roadmap to Reducing Animal Testing in Preclinical Safety Studies.
https://www.fda.gov/files/newsroom/published/roadmap_to_reducing_animal_testing_in_preclinical_safety_studies.pdf

Phasing out animal testing will enhance drug safety and efficiency by replacing outdated requirements.sciencedirect.com
Arrowsmith, J., et al. (2025). The FDA's plan to phase out animal testing. Trends in Biotechnology.
https://www.sciencedirect.com/science/article/pii/S0167779925005323?dgcid=rss_sd_all